

WHAT IS CLAIMED IS:

1. An antibody or antigen binding portion thereof that specifically binds to c-MET, wherein said antibody comprises a c-MET antibody selected from the group consisting of PGIA-01-A1, PGIA-01-A2, PGIA-01-A3, PGIA-01-A4, PGIA-01-A5, PGIA-01-A6, PGIA-01-A7, PGIA-01-A8, PGIA-01-A9, PGIA-01-A10, PGIA-01-A11, PGIA-01-A12, PGIA-01-B1, PGIA-01-B2, PGIA-02-A1, PGIA-02-A2, PGIA-02-A3, PGIA-02-A4, PGIA-02-A5, PGIA-02-A6, PGIA-02-A7, PGIA-02-A8, PGIA-02-A9, PGIA-02-A10, PGIA-02-A11, PGIA-02-A12, PGIA-02-B1, PGIA-03-A1, PGIA-03-A2, PGIA-03-A3, PGIA-03-A4, PGIA-03-A5, PGIA-03-A6, PGIA-03-A7, PGIA-03-A8, PGIA-03-A9, PGIA-03-A10, PGIA-03-A11, PGIA-03-A12, PGIA-03-B1, PGIA-03-B2, PGIA-03-B3, PGIA-03-B4, PGIA-03-B5, PGIA-03-B6, PGIA-03-B7, PGIA-03-B8, PGIA-04-A1, PGIA-04-A2, PGIA-04-A3, PGIA-04-A4, PGIA-04-A5, PGIA-04-A6, PGIA-04-A7, PGIA-04-A8, PGIA-04-A9, PGIA-04-A10, PGIA-04-A11, PGIA-04-A12, and PGIA-05-A1 or fragment of any one thereof.
2. The antibody or antigen binding portion thereof according to claim 1 wherein said c-Met antibody is selected from the group consisting of PGIA-01-A8, PGIA-03-A9, PGIA-03-A11, PGIA-03-B2, PGIA-04-A5, PGIA-04-A8, PGIA-05-A1 or a fragment of any one thereof.
3. The antibody or antigen binding portion thereof according to claim 1 wherein said c-Met antibody is selected from the group consisting of PGIA-03-A9, PGIA-04-A5, and PGIA-04-A8 or a fragment of any one thereof.
4. The antibody or antigen binding portion thereof of claim 1, wherein said antibody comprises at least one light chain of said c-Met antibody.
5. The antibody or antigen binding portion thereof of claim 1, wherein said antibody comprises at least one heavy chain of said c-Met antibody.
6. The antibody or antigen binding portion thereof of claim 4 or 5, wherein said antibody comprises at least one CDR of said c-Met antibody.
7. The antibody or antigen binding portion thereof of claim 6, wherein said antibody comprises all of the CDRs of at least one heavy chain of said c-Met antibody.

8. The antibody or antigen binding portion thereof of claim 6, wherein said antibody comprises all of the CDRs of at least one light chain of said c-Met antibody.

5 9. The antibody or antigen binding portion thereof of claim 6, wherein said antibody comprises all of the CDRs of a heavy chain and a light chain of said c-Met antibody.

10 10. The antibody or antigen binding portion thereof of claim 6, wherein said antibody comprises CDRs from different light chains of said c-Met antibody.

11. The antibody or antigen binding portion thereof of claim 6, wherein said antibody comprises CDRs from different heavy chains of said c-Met antibody.

12. The antibody or antigen binding portion thereof of claim 6, wherein said antibody comprises a V_L and/or V_H variable region of said c-Met antibody.

13. The antibody or antigen binding portion thereof according to claim 1, wherein said c-Met antibody comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, and SEQ ID NO:60, or a fragment of any one thereof.

14. The antibody or antigen binding portion thereof of claim 13, wherein said antibody comprises at least one light chain of said c-Met antibody.

15. The antibody or antigen binding portion thereof of claim 13, wherein said antibody comprises at least one heavy chain of said c-Met antibody.

5 16. The antibody or antigen binding portion thereof of claim 14 or 15, wherein said antibody comprises at least one CDR of said c-Met antibody.

17. The antibody or antigen binding portion thereof of claim 16, wherein said antibody comprises all the CDRs of at least one heavy chain of said c-Met antibody.

10 18. The antibody or antigen binding portion thereof of claim 16, wherein said antibody comprises all the CDRs of at least one light chain of said c-Met antibody.

19. The antibody or antigen binding portion thereof of claim 16, wherein said antibody comprises all of the CDRs of a heavy chain and a light chain of said c-Met antibody.

15 20. The antibody or antigen binding portion thereof of claim 16, wherein said antibody comprises CDRs from different light chains of said c-Met antibody.

20 21. The antibody or antigen binding portion thereof of claim 16, wherein said antibody comprises CDRs from different heavy chains of said c-Met antibody.

22. The antibody or antigen binding portion thereof of claim 16, wherein said antibody comprises at least one V_L and/or V_H variable region of said c-Met antibody.

25 23. The antibody or antigen-binding portion thereof according to any one of claims 1 or 13, wherein the antibody or portion thereof has at least one property selected from the group consisting of:

30 a) cross-competes for binding to human c-Met with the c-Met antibody selected from the group consisting of PGIA-01-A1, PGIA-01-A2, PGIA-01-A3, PGIA-01-A4, PGIA-01-A5, PGIA-01-A6, PGIA-01-A7, PGIA-01-A8, PGIA-01-A9, PGIA-01-A10, PGIA-01-A11, PGIA-01-A12, PGIA-01-B1, PGIA-01-B2, PGIA-02-A1, PGIA-02-A2, PGIA-02-A3, PGIA-02-A4, PGIA-02-A5, PGIA-02-A6, PGIA-02-A7, PGIA-02-A8, PGIA-02-A9, PGIA-02-A10, PGIA-02-A11, PGIA-02-A12, PGIA-02-B1, PGIA-03-A1, PGIA-03-A2, PGIA-03-

A3, PGIA-03-A4, PGIA-03-A5, PGIA-03-A6, PGIA-03-A7, PGIA-03-A8, PGIA-03-A9, PGIA-03-A10, PGIA-03-A11, PGIA-03-A12, PGIA-03-B1, PGIA-03-B2, PGIA-03-B3, PGIA-03-B4, PGIA-03-B5, PGIA-03-B6, PGIA-03-B7, PGIA-03-B8, PGIA-04-A1, PGIA-04-A2, PGIA-04-A3, PGIA-04-A4, PGIA-04-A5, PGIA-04-A6, PGIA-04-A7, PGIA-04-A8, PGIA-04-A9, PGIA-04-A10, PGIA-04-A11, PGIA-04-A12, and PGIA-05-A1;

b) binds to the same epitope of human c-Met as the c-Met antibody selected from the group consisting of PGIA-01-A1, PGIA-01-A2, PGIA-01-A3, PGIA-01-A4, PGIA-01-A5, PGIA-01-A6, PGIA-01-A7, PGIA-01-A8, PGIA-01-A9, PGIA-01-A10, PGIA-01-A11, PGIA-01-A12, PGIA-01-B1, PGIA-01-B2, PGIA-02-A1, PGIA-02-A2, PGIA-02-A3, PGIA-02-A4, PGIA-02-A5, PGIA-02-A6, PGIA-02-A7, PGIA-02-A8, PGIA-02-A9, PGIA-02-A10, PGIA-02-A11, PGIA-02-A12, PGIA-02-B1, PGIA-03-A1, PGIA-03-A2, PGIA-03-A3, PGIA-03-A4, PGIA-03-A5, PGIA-03-A6, PGIA-03-A7, PGIA-03-A8, PGIA-03-A9, PGIA-03-A10, PGIA-03-A11, PGIA-03-A12, PGIA-03-B1, PGIA-03-B2, PGIA-03-B3, PGIA-03-B4, PGIA-03-B5, PGIA-03-B6, PGIA-03-B7, PGIA-03-B8, PGIA-04-A1, PGIA-04-A2, PGIA-04-A3, PGIA-04-A4, PGIA-04-A5, PGIA-04-A6, PGIA-04-A7, PGIA-04-A8, PGIA-04-A9, PGIA-04-A10, PGIA-04-A11, PGIA-04-A12, and PGIA-05-A1;

c) binds to human c-Met with substantially the same K_d as the c-Met antibody selected from the group consisting of PGIA-01-A1, PGIA-01-A2, PGIA-01-A3, PGIA-01-A4, PGIA-01-A5, PGIA-01-A6, PGIA-01-A7, PGIA-01-A8, PGIA-01-A9, PGIA-01-A10, PGIA-01-A11, PGIA-01-A12, PGIA-01-B1, PGIA-01-B2, PGIA-02-A1, PGIA-02-A2, PGIA-02-A3, PGIA-02-A4, PGIA-02-A5, PGIA-02-A6, PGIA-02-A7, PGIA-02-A8, PGIA-02-A9, PGIA-02-A10, PGIA-02-A11, PGIA-02-A12, PGIA-02-B1, PGIA-03-A1, PGIA-03-A2, PGIA-03-A3, PGIA-03-A4, PGIA-03-A5, PGIA-03-A6, PGIA-03-A7, PGIA-03-A8, PGIA-03-A9, PGIA-03-A10, PGIA-03-A11, PGIA-03-A12, PGIA-03-B1, PGIA-03-B2, PGIA-03-B3, PGIA-03-B4, PGIA-03-B5, PGIA-03-B6, PGIA-03-B7, PGIA-03-B8, PGIA-04-A1, PGIA-04-A2, PGIA-04-A3, PGIA-04-A4, PGIA-04-A5, PGIA-04-A6, PGIA-04-A7, PGIA-04-A8, PGIA-04-A9, PGIA-04-A10, PGIA-04-A11, PGIA-04-A12, and PGIA-05-A1; and

d) binds to human c-MET with substantially the same off rate as the c-Met antibody selected from the group consisting of PGIA-01-A1, PGIA-01-A2, PGIA-01-A3, PGIA-01-A4, PGIA-01-A5, PGIA-01-A6, PGIA-01-A7, PGIA-01-A8, PGIA-01-A9, PGIA-01-A10, PGIA-01-A11, PGIA-01-A12, PGIA-01-B1, PGIA-01-B2, PGIA-02-A1, PGIA-02-A2, PGIA-02-A3, PGIA-02-A4, PGIA-02-A5, PGIA-02-A6, PGIA-02-A7, PGIA-02-A8, PGIA-02-A9, PGIA-02-A10, PGIA-02-A11, PGIA-02-A12, PGIA-02-B1, PGIA-03-A1, PGIA-03-A2, PGIA-03-A3, PGIA-03-A4, PGIA-03-A5, PGIA-03-A6, PGIA-03-A7, PGIA-03-A8, PGIA-03-A9, PGIA-03-A10, PGIA-03-A11, PGIA-03-A12, PGIA-03-B1, PGIA-03-B2, PGIA-03-B3, PGIA-03-B4, PGIA-03-B5, PGIA-03-B6, PGIA-03-B7, PGIA-03-B8, PGIA-04-A1, PGIA-04-A2, PGIA-04-A3, PGIA-04-A4, PGIA-04-A5, PGIA-04-A6, PGIA-04-A7, PGIA-04-A8, PGIA-04-A9, PGIA-04-A10, PGIA-04-A11, PGIA-04-A12, and PGIA-05-A1.

24. The antibody or antigen-binding portion thereof according to claim 1 or 13, wherein said antibody or antigen-binding portion thereof comprises a variable region of a light chain, wherein the sequence of said variable region of said light chain comprises no more than ten amino acid changes from the amino acid sequence encoded by a germline gene thereof.

25. The antibody or antigen-binding portion thereof according to any one of claims 1 or 13 that is

- a) an immunoglobulin G (IgG), an IgM, an IgE, an IgA or an IgD molecule;
- b) an Fab fragment, an F(ab')₂ fragment, an Fv fragment, a single chain antibody; or
- c) a humanized antibody, a human antibody, a chimeric antibody or a bispecific antibody.

26. The antibody of claim 25 a) wherein said c-Met antibody is an IgG selected from the group consisting of 11978, 11994, 12075, 12119, 12123, 12133, and 12136.

27. The antibody of claim 26 selected from the group consisting 11994, 12133, and 12136.

28. The antibody of claim 25 b) wherein said c-Met antibody is a Fab selected from the group consisting of 11978, 11994, 12075, 12119, 12123, 12133, and 12136.

5 29. The antibody of claim 28 selected from the group consisting of 11994, 12133, and 12136.

30. A pharmaceutical composition comprising the antibody or portion thereof according to claim 1 and a pharmaceutically acceptable carrier.

31. An isolated cell line that produces the antibody according to claim 1.

10 32. A method of diagnosing the presence or location of an HGF expressing tumor in a subject in need thereof, comprising the steps of

- a) injecting the antibody according to claim 1 into the subject,
- b) determining the expression of c-MET in the subject by localizing where the antibody has bound,
- 15 c) comparing the expression in part (b) with that of a normal reference subject or standard, and
- d) diagnosing the presence or location of the tumor.

20 33. A method of treating cancer in a human with the antibody or antigen-binding portion thereof according to claim 1, comprising the step of administering to said human an effective amount of said antibody.

34. An isolated nucleic acid molecule that comprises a nucleic acid sequence that encodes a heavy chain or antigen-binding portion thereof or a light chain or antigen-binding portion thereof of an antibody according to claim 1.

25 35. The nucleic acid sequence according to claim 34 wherein said nucleic acid sequences is selected from the group consisting of: SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, 30 SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID

NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, and SEQ ID NO:120 or a fragment thereof.

36. A vector comprising the nucleic acid molecule according to claim 34 or 35, wherein the vector optionally comprises an expression control sequence operably linked to the nucleic acid molecule.

37. A host cell transformed or transfected with the nucleic acid sequence of claim 34 or 35.

38. The antibody or antigen binding portion thereof of claim 1, wherein said antibody or antigen binding portion is a partial agonist against c-MET.

39. The antibody or antigen binding portion thereof of claim 1, wherein said antibody or antigen binding portion blocks HGF driven proliferation.

40. The antibody or antigen binding portion thereof of claim 1, wherein said antibody or antigen binding portion blocks HGF binding to human c-MET.